UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/183,789	10/30/1998	VALERIE MARTELANGE	L0461/7047	3523

7590 06/18/2003

JOHN R VAN AMSTERDAM
WOLF GREENFIELD & SACKS
600 ATLANTIC AVENUE
BOSTON, MA 02210

EXAMINER
HARRIS, ALANA M

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/18/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/183,789	Applicant(s) MARTELANGE ET AL.	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,9,18-20,24,28,35,38,40,41,45,47 and 50-60* is/are pending in the application.

4a) Of the above claim(s) *20,24,28,35,38,45,47 and 287* is/are withdrawn from consideration.

5)☐ Claim(s) *8,41 and 43* is/are allowed.

6)☒ Claim(s) *1,9,19,40 and 60* is/are rejected.

7)☐ Claim(s) *18 and 50-59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 11, 2002 has been entered.

2. Claims 1, 8, 9, 18-20, 24, 28, 35, 38, 40, 41, 43, 45, 47 and 50-60 are pending.

Claims 1, 9, 40, 41, 57 and 58 have been amended.

Claims 20, 24, 28, 35, 38, 45 and 47, drawn to non-elected inventions are withdrawn from examination.

Claims 1, 8, 9, 18, 19, 40, 41, 43 and 50-60 are examined on the merits.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claim 40 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in light of the claim amendment.

4. The rejection of claims 9, 41, 57 and 58 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Claim Rejections - 35 USC § 102

5. The rejection of claims 1, 9, 18 and 19 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,880,102 (filed Jan. 17, 1995) is withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 9 and 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants assert that support for the amendment to claim 9 can be found in the specification at page 14, lines 28-30. The Examiner has reviewed this section of the specification and notes that the segments can be 12 and 32 nucleotides or more in length and up to the entire length of the disclosed sequence. In this particular case

SEQ ID NO: 38 is 2021 base pairs. The specification does not support a fragment exclusively between 12 and 1996 nucleotides in length. Likewise, SEQ ID NO: 43 is 2463 base pairs in length and Applicants' claim limits the fragment to between 12 and 2441 nucleotides in length. It is not clear how the text found on the pages cited by the Applicants supports the language found within claim 9.

Furthermore, Applicants assert that the amendment to claim 40 is supported within the specification at page 14, lines 21-24. This passage contemplates the use of antisense molecules to inhibit the expression of SAGE (SEQ ID NO: 38) or sdp3.5 (SEQ ID NO: 40 and 43) with respect to therapeutic purposes, which is regarded as reading on *in vivo* therapy. Applicants are requested to pointedly express where support can be found in the specification for implementation of the claimed composition *in vitro*.

If the claim is further amended to delete the term, in vitro the 112, 1st enablement rejection of record present on page 5, paragraph 7 in the first action on the merits as Paper number 12 will be set forth.

8. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants broadly claim a host cell comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, 40, 38 and 43SEQ ID NO: 4 contained within an expression vector and a method for producing the said polypeptide by

culturing the said cell. This claim reads on a cell within a transgenic animal given that the term "isolated" is not denoted in describing the host cell. The breadth of the claim reads on the implementation of the host cell in both *in vitro* and *in vivo* assays.

The state of the art at the time of filing was such that one of skill could not predict the phenotype of transgenics. For example, Overbeek (1994, "Factors affecting transgenic animal production," Transgenic animal technology, pages 96-98) taught that within one litter of transgenic mice, considerable variation in the level of transgene expression occurs between founder animals and causes different phenotypes (page 96, last paragraph). The art of transgenic animals has for many years stated that the unpredictability lies, in part, with the site or sites of transgene integration into the target genome and that "the position effect" as well as unidentified control elements are recognized to cause aberrant expression of a transgene (Wall, 1996 Theriogenology, Vol. 45, pp. 57-68). The elements of the particular construct used to make transgenic animals are also held to be critical, and they must be designed case by case without general rules to obtain good expression of a transgene; e.g., specific promoters, presence or absence of introns, etc. (Houdebine, 1994, J. Biotech. Vol. 34, pages 269-287, specifically page 281). Furthermore, transgenic animals are regarded to have within their cells, cellular mechanisms that prevent expression of the transgene, such as methylation or deletion from the genome (Kappell, 1992, Current Opinions in Biotechnology, Vol. 3, pp. 548-553).

Well-regulated transgene expression is not frequently achieved because of poor levels or the complete absence of expression or leaky expression in non-target tissues

(Cameron, 1997, Molec. Biol. 7, pages 253-265, specifically page 256, col. 1 -2, bridg. parag.). Factors influencing low expression, or the lack thereof, are not affected by copy number and such effects are seen in lines of transgenic mice made with the same construct (Cameron, 1997, Molec. Biol. 7, page 256, lines 3-9). With regard to the importance of promoter selection, Niemann (1997) states that transgenic pigs made with different promoters regulating expression of a growth hormone gene give disparate phenotypes - one deleterious to the pig, the other compatible with pig health (Niemann, 1997, Transg. Res. 7, pages 73-75, specifically page 73, col. 2, parag. 2, line 12 to page 73, col. 1, line 4).

Examples in the literature aptly demonstrate that even closely related species carrying the same transgene construct can exhibit widely varying phenotypes. Mullins(1993, Hypertension, Vol. 22, pp. 630-633) states that not all animals express a transgene sufficiently to provide a model for a disease as the integration of a transgene into different species of animal has been reported to give divergent phenotypes. For example, several animal models of human diseases have relied on transgenic rats when the development of mouse models was not feasible. Mullins (1990, Nature, Vol. 344, 541-544) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse *Ren-2* renin transgene. Hammer (1990, Cell, Vol. 63, 1099-1112) describes spontaneous inflammatory disease in inbred Fischer and Lewis rats expressing human class I major histocompatibility allele HLA-B27 and human β_2-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice expressing the same transgenes that

successfully caused the desired symptoms in transgenic rats (Mullins, 1989, EMBO J., vol. 8, pages 4065-4072; Taurog, 1988, Jour. Immunol., Vol. 141, pages 4020-4023). Mullins (1996, J. Clin. Invest. Vol. 98, pages S37-S40) disclose that the use of nonmurine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to another. Thus, at the time of filing, the phenotype of a transgenic cell contained within any animal was unpredictable and could not be prepared for any species. Applicants can obviate the instant rejection by amending the claims to recite the term "isolated" before the recitation, "host cell".

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1, 40 and 60 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "hybridize under stringent conditions" in claims 1, 40 and 60 are vague and indefinite. The metes and bounds are unclear in the absence of limitation specifying specific stringency conditions.

b. Claim 40 is vague and indefinite in the recitation "an antisense nucleic acid which binds *in vitro* to a tumor associated nucleic acid which hybridizes under stringent conditions to a nucleic acid molecule selected from the group consisting of SEQ ID NO: 38 and SEQ ID NO: 43". It is not clear if the antisense nucleic acid **or** the

tumor associated nucleic acid hybridizes to the nucleic acid having the sequence of SEQ ID NO: 38 or SEQ ID NO: 43. Applicants are requested to clarify the claim.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
June 16, 2003